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08 April 2009

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Published Version

Peer-review status of attached file:

Peer-reviewed

Citation for published item:

Sawdon, M. and Kirkman, E. and Watkins, P. (2000) 'Doxapram attenuates the apnoea induced by primary thoracic blast injury in the anaesthetised rat.', The journal of physiology., 528 P . p. 104.

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Doxapram attenuates the apnoea induced by primary thoracic blast injury in the anaesthetized rat

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Primary blast injury to the thorax induces a bradycardia, hypotension and apnoea (Guy *et al.* 1998). This response is a reflex with vagal afferent and/or efferent pathways (Ohnishi *et al.* 1998). The bradycardia can be abolished by atropine, although we know of no pharmacological means of attenuating the apnoea. Doxapram is an analeptic (O'Connor *et al.* 1996) with pressor actions (Huon *et al.* 1998). This study aimed to determine whether doxapram could modify the early respiratory and cardiovascular responses to thoracic blast injury.

Male Wistar rats (243–314 g body weight) were used in two groups of eight. Surgical anaesthesia was induced and maintained with isoflurane (3·0–3·5% in O_2–N_2O, $F_{I,O_2} = 0{\cdot}5$). On completion of surgery anaesthesia was maintained with alphadolone/alphaxalone (19–21 mg kg^{-1} h^{-1} I.V.). Heart period (HP) was measured from the electrocardiogram, arterial blood pressure via the ventral tail artery and body temperature via a rectal probe. Respiratory tidal volume (V_T) and rate (RR) were measured via a pneumotachograph connected to a tracheal cannula. Respiratory minute volume (RMV) was calculated as the product of V_T and RR. Body temperature was maintained at 38·0 °C using external heating. At the end of the study the animals were killed with an overdose of anaesthetic.

Both groups received a blast wave focused on the ventral thorax (Guy *et al.* 1998) shown previously to generate an overpressure of 3 atm at the thorax. One to three seconds after blast, Group I received 0·9% saline (1 ml kg^{-1} I.V. bolus) while Group II received doxapram (10 mg kg^{-1}, 1 ml kg^{-1} I.V.). In Group I blast produced an apnoea lasting 24·4 ± 2·4 s (mean ± S.E.M.), a significant fall in mean arterial blood pressure (MBP from 120 ± 4 to 34 ± 2 mmHg, $P < 0{\cdot}05$, repeated measures ANOVA) and a significant increase in HP (from 140 ± 5 to 429 ± 27 ms). RMV returned to pre-blast levels while MBP recovered partially to 97 ± 5 mmHg over the subsequent 20 min. Doxapram (Group II) significantly reduced the duration of apnoea (6·8 ± 0·5 s) and attenuated the hypotension (MBP falling from 116 ± 5 to 58 ± 5 mmHg), but did not alter the bradycardic response. Thereafter RMV was significantly higher in Group II than in Group I (219 ± 19 *vs.* 143 ± 19 ml min^{-1}) for 2 min after blast, while MBP was significantly higher for 10 min after blast in Group II.

These results indicate that doxapram is effective in attenuating the apnoea and hypotension induced by thoracic blast injury.

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This work was supported by DERA, Porton Down, UK.